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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/642,236	08/17/2000	George R. Schwartz	41145-1001	6972

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 08/04/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/642,236	SCHWARTZ, GEORGE R.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-61* is/are pending in the application.

4a) Of the above claim(s) *23-32* is/are withdrawn from consideration.

5)☒ Claim(s) *61* is/are allowed.

6)☒ Claim(s) *33,34,39-46 and 51-60* is/are rejected.

7)☒ Claim(s) *35-38 and 47-50* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 23-61 are pending.

Applicants' amendment filed on June 3, 2003 (Paper No. 18) is acknowledged. Applicants' response has been fully considered. Claims 35, 37-39, 47 and 49-51 have been amended, claims 23-32 are non-elected claims and stand withdrawn from consideration. Thus, claims 33-61 are examined.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

2. The previous rejection of claims 35-70 under 35 USC § 112, second paragraph, is withdrawn in view of applicants' amendment to the claim, and applicants' response at page 7 in Paper No. 18.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 33, 34, 39-46 and 51-60 as presented in the amendment filed Jun3 3, 2003 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing regeneration and repair of nerve axon myelin coatings in a mammal, or a method of inducing increased platelet production with secondary increased endogenous production of platelet-derived growth factor (PDGF) to produce the effect of regenerating nerve axon myelin coatings in a mammal, the method comprising systemically administering

thrombopoietin and thyroid hormone, or, thrombopoietin, thyroid hormone and thyrotropin, does not reasonably provide enablement for a method as indicated above by administering thrombopoietin alone, or thrombopoietin and a thyroid regulatory agent, wherein the thyroid regulatory agent is not identified. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope to claims where administering thrombopoietin alone, or where the thyroid regulatory agent is not identified.

Claims 33, 34, 39-46 and 51-60 are directed to a method of inducing regeneration and repair of nerve axon myelin coatings in a mammal, comprising systemically administering thrombopoietin and a thyroid regulatory agent (claims 33-34 and 39-44); a method of inducing increased platelet production with secondary increased endogenous production of platelet-derived growth factor in a mammal, the method comprising systemically administering thrombopoietin alone (claims 57-60), or thrombopoietin and a thyroid regulatory agent (claims 45, 46, 51-56). The specification, however, only discloses cursory conclusions without data supporting the findings, which states that the present invention provides a method for neuron and myelin regeneration using endogenous PDGF which is induced by use of an enhancement agent such as thrombopoietin, and a regulatory agent such as thyroid hormone, thyrotropin and the like may be combined with the enhancement agent to regulate cell division and oligogendroglia production (pages 4-7). There are no indicia that the present application enables the full scope in view of a method of inducing regeneration and repair of nerve axon myelin coating or a method of inducing increased platelet production using thrombopoietin, or thrombopoietin and a regulatory agent as discussed in the stated rejection. The present application provides no indicia

and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding thyroid regulatory agents, and the treating conditions for inducing regeneration and repair of nerve axon myelin coatings, or for inducing increased platelet production with secondary increased endogenous production of PDGF to produce the effect of regeneration of nerve axon myelin coatings using the thyroid regulatory agent with thrombopoietin, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no working examples indicating the claimed methods in association with variants except for using thrombopoietin with thyroid hormone and thyrotropin, or, thrombopoietin and thyroid hormone (Examples 1-3).

(3). The state of the prior art and relative skill of those in the art:

The prior art, for example, Thomas (U. S. Patent 5,879,673) teaches administration of thrombopoietin at single or multiple doses is used to increase the number of platelet for treating thrombocytopenia; Grinspan *et al.* (Annals of neurology 36, S140-S142 (supplement) 1994)

teach PDGF stimulates the formation of oligodendroglia from partially differentiated progenitor cells, and loss of oligodendroglia is frequently found in deamyelinative diseases; Rodriguez-Pena (J. Neurobiol. 40, 497-512 (1997)) teaches thyroid hormone regulates the number of oligodendrocyte generated by directly promoting their differentiation. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the identities of various thyroid regulatory agents other than thyorid hormone and thyrotropin, the treating conditions using these agents, and the effect of thrombopoietin alone to be considered enabling for the claimed method.

(4). Predictability or unpredictability of the art:

The specification has shown using thrombopoietin with thyroid hormone and thyrotropin, or, thrombopoietin and thyroid hormone to induce regeneration and repair of nerve axon myelin coatings in an animal model (Examples 1-3). However, the specification does not provide the treating conditions using various thyroid regulatory agents nor indicates the effects of these agents in combination with thrombopoietin, or the effect using thrombopoietin alone, thus the outcome of the treatment is highly unpredictable in mammals.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method of inducing regeneration and repair of nerve axon myelin coatings in a mammal, comprising systemically administering thrombopoietin and a thyroid regulatory agent; a method of inducing increased platelet production with secondary increased endogenous production of platelet-derived growth factor to produce the effect of regeneration of nerve axon myelin coatings in a mammal, comprising systemically administering

thrombopoietin alone, or thrombopoietin and a thyroid regulatory agent. However, the specification has only shown using thrombopoietin with thyroid hormone and thyrotropin, or, thrombopoietin and thyroid hormone to induce regeneration and repair of nerve axon myelin coatings in animal models (Examples 1-3). There is no working example demonstrating the use of thrombopoietin alone, or thrombopoietin with any other thyroid regulatory agent than thyroid hormone in inducing regeneration and repair of nerve axon myelin coatings, or being able to produce the desired effect in a mammal. The specification has not provided the treating conditions such as the effective amount of a thyroid regulatory agent other than thyroid hormone, nor indicated the effects of these agents. Furthermore, there is no data indicating thrombopoietin alone would produce the desired effect. Since the specification fails to provide sufficient guidance on the identities of various thyroid regulatory agents, and the treating conditions and the effects of these agents, it is necessary to carry out further experimentation to assess the effects of various thyroid regulatory agents in inducing regeneration and repair of nerve axon myelin coatings in vivo.

(6). Nature of the Invention

The scope of the claims encompass using thrombopoietin, or thrombopoietin and a thyroid regulatory agent to induce regeneration and repair of nerve axon myelin coatings in a mammal, but the specification does not provide the treating conditions and the effects for various thyroid regulatory agents or thrombopoietin alone in the claimed method. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working example does not demonstrate the claimed methods associated with variants, the art is unpredictable regarding the effects of

using various thyroid regulatory agents or thrombopoietin alone, and the teachings in the specification are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the therapeutic effects of using thrombopoietin alone or in conjunction with various thyroid regulatory agents.

In response, applicants indicate the invention is directed to employ thrombopoietin to increase endogenous PDGF by increasing platelet concentrations either with a thyroid regulatory agent or without a thyroid regulatory agent, which in turn effect myelin repair or regeneration, and it has been reported that thrombopoietin administered to normal subject results in an increase in platelet counts, however, no medical condition was described for which increasing platelet counts above normal ranges was desirable (page 7 of the response); The prior art has shown PDGF could be used to induce myelin repair or generation, and it was known that various regulatory agents such as thyroid hormone and thyrotropin may be employed to effect cell division rates and induction of differentiation, especially of oligodendrocytes cells (pages 7-8 of the response). The office action do not demonstrate either the requisite factual predicate for an enablement rejection or "undue experimentation" would be required, and there are no examples or references suggest there is any uncertainty as to the effect of thrombopoietin to increase platelet levels which would result in increased PDGF. Regarding thyroid regulatory agents, which are employed in the invention as to adjunct to thrombopoietin, and the scientific literature and teachings of the patent are sufficient (page 9 of the response). The response has been fully considered, however, the argument is not found persuasive because the prior art only indicates thrombopoietin administered to normal subject results in an increase in platelet counts, and PDGF could be used to induce myelin repair or generation, however, the prior art does not teach

the correlation between amount of thrombopoietin administered and the amount of PDGF produced either in vitro or in vivo, and the specification has not demonstrated the administration of sufficient amount of thrombopoietin alone would produce effective amount of PDGF to induce myelin repair or generation in vitro or in vivo, nor has indicated the effect of administering thrombopoietin alone in animal models. Regarding thyroid regulatory agents, all the references only indicate the effect of thyroid hormone on the induction of differentiation of oligodendrocytes cells, the prior art does not teach the same effects induced by any other thyroid regulatory agents. Since the prior art and the specification do not provide sufficient teaching/guidance for enabling the full scope of the claims, it is required to carry out additional experimentation to assess the effects of variants used in the claimed method.

4. Claims 35-38 and 47-50 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

5. Claims 33, 34, 39-46 and 51-60 are rejected, and claims 35-38 and 47-50 are objected to. It appears claim 61 is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers

for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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August 1, 2003

Christopher S. F. Low

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